Claims

1. Use of Aan antithrombotic molecule having both antiplatelet and anticoagulant (APAC) activity comprising a human plasma protein to which there is attached, via a plurality of linker molecules, a plurality of heparin chains selected from the group comprising 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, and 16, each chain having a MW in the range 10-21 KDa for the manufacture of a medicament foruse in the prevention and/or treatment of thrombocytopenia, wherein said thrombocytopenia is selected from the group comprising, including any combination thereof: heparin-induced thrombocytopenia (HIT) type I; heparin-induced thrombocytopenia (HIT) type II; heparin-induced thrombocytopenia and thrombosis (HITT); heparin-independent thrombocytopenia aHIT; and in vaccine-induced thrombocytopenia and thrombosis (VITT).

2. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to claim 1 wherein said thrombocytopenia is selected from the group comprising, including any combination thereof: heparin-induced thrombocytopenia (HIT) type I; heparin-induced thrombocytopenia (HIT) type II; heparin-induced thrombocytopenia and thrombosis (HITT); heparin-independent thrombocytopenia aHIT; and in vaccine-induced thrombocytopenia and thrombosis (VITT).

3.2. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to claim 1 wherein said thrombocytopenia is selected from the group comprising: heparin-induced thrombocytopenia (HIT) type II; and heparin-induced thrombocytopenia and thrombosis (HITT).

4.3. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to claim 1 wherein said thrombocytopenia is immunologically-based and selected from the group comprising: heparin-induced thrombocytopenia (HIT) type II; heparin-induced thrombocytopenia and thrombosis (HITT); heparin-independent thrombocytopenia aHIT; and in vaccine-induced thrombocytopenia and thrombosis (VITT).

5.4. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to claim 1 wherein said thrombocytopenia is non-immunologically-based and selected from the group comprising: heparin-induced

thrombocytopenia (HIT) type I; heparin-induced thrombocytopenia and thrombosis (HITT); and in vaccine-induced thrombocytopenia and thrombosis (VITT).

~~6.~~5. The ~~antithrombotic molecule for~~ use ~~in the prevention and/or treatment of thrombocytopenia~~ according to claim 1 wherein said thrombocytopenia is caused by heparin and selected from the group comprising: heparin-induced thrombocytopenia (HIT) type I; heparin-induced thrombocytopenia (HIT) type II; thrombocytopenia and thrombosis (HITT); and in vaccine-induced thrombocytopenia and thrombosis (VITT).

~~7.~~6. The ~~antithrombotic molecule for~~ use ~~in the prevention and/or treatment of thrombocytopenia~~ according to any one of claims 1 – 5~~6~~ wherein said APAC molecule has 4, 5 or 6, heparin chains attached to said plasma protein.

~~8.~~7. The ~~antithrombotic molecule for~~ use ~~in the prevention and/or treatment of thrombocytopenia~~ according to any one of claims 1 - 6~~7~~ wherein said APAC molecule has 5 heparin chains attached to said plasma protein.

~~9.~~8. The ~~antithrombotic molecule for~~ use ~~in the prevention and/or treatment of thrombocytopenia~~ according to any one of claims 1 - 7~~8~~ wherein said APAC is formulated for administration at a dose, in blood or plasma, within the range 0.15 µg/ml - 10 µg/ml, including all 0.1 µg/ml there between.

~~10.~~9. The ~~antithrombotic molecule for~~ use ~~in the prevention and/or treatment of thrombocytopenia~~ according to claim 8~~9~~ wherein said APAC is formulated for administration at a dose within the range 1 µg/ml - 3 µg/ml, including all 0.1 µg/ml there between.

~~11.~~10. The ~~antithrombotic molecule for~~ use ~~in the prevention and/or treatment of thrombocytopenia~~ according to any one of claims 1 - 7~~8~~ wherein said APAC is formulated for administration at a dose within the range 0.1 – 0.3 mg/kg.

~~12.~~11. The ~~antithrombotic molecule for~~ use ~~in the prevention and/or treatment of thrombocytopenia~~ according to any one of the preceding claims wherein said human plasma protein is selected from the group comprising or consisting of: albumin, globulin or fibrinogen.

~~13.~~12. The ~~antithrombotic molecule for~~ use ~~in the prevention and/or treatment of thrombocytopenia~~ according to claim 11~~2~~ wherein said human plasma protein is serum albumin or alpha2-macroglobulin.

14.13. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to any one of the preceding claims wherein said human plasma protein is recombinant.

15.14. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to any one of the preceding claims wherein said heparin is unfractionated heparin.

16.15. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to any one of the preceding claims wherein said heparin has a MW of 15 or 16 or 17 KDa.

17.16. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to any one of the preceding claims wherein said heparin is recombinant.

18.17. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to any one of the preceding claims wherein each linker molecule binds one molecule of heparin to said human plasma protein.

19.18. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to any one of the preceding claims wherein said linker is an amine linker and so links with amino groups on said heparin and plasma protein.

20.19. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to any one of the preceding claims wherein said linker conjugates with serine on the heparin chain and a lysine on the plasma protein.

21.20. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to any one of the preceding claims wherein said linker is a hetero-bi-functional cross-linker such as a 3-(2-Pyridyldithio)propionic acid N-hydroxysuccinimide ester (SPDP) linker or a homo-bi-functional cross-linker such as a 3,3'-Dithiodipropionicacid di(N-hydroxysuccinimide (NHS)-ester (DTSP) linker.

22.21. The antithrombotic molecule for use in the prevention and/or treatment of thrombocytopenia according to any one of the preceding claims wherein said APAC has a coupling level (CL) of 5 heparins per human serum albumin (HSA) and the linker used for the coupling is SPDP.

23. A method for the prevention and/or treatment thrombocytopenia;

wherein an effective amount of antithrombotic molecule is administered to an individual to be treated, said antithrombotic molecule having both antiplatelet and anticoagulant (APAC) activity comprising a human plasma protein to which there is attached, via a plurality of linker molecules, a plurality of heparin chains each having a MW between10-21 KDa and further wherein the number of said heparin chains attached to said plasma protein is selected from the group comprising 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, and 16.

24. The method according to claim 23 wherein said thrombocytopenia is selected from the group comprising, including any combination thereof: heparin-induced thrombocytopenia (HIT) type I; heparin-induced thrombocytopenia (HIT) type II; heparin-induced thrombocytopenia and thrombosis (HITT); heparin-independent thrombocytopenia aHIT; and in vaccine-induced thrombocytopenia and thrombosis (VITT).

25. The method according to claim 23 or claim 24 wherein said APAC is administered at a dose, in blood or plasma, within the range including and between 0.15 µg/ml - 10 µg/ml, including all 0.1µg/ml there between.

26. The method according to claim 25 wherein said APAC is administered at a dose within the range 1 µg/ml - 3 µg/ml, including all 0.1 µg/ml there between.

27. The method according to claim 23 or claim 24 wherein said APAC is administered at a dose in the range of 0.1 – 0.3 mg/kg.